REMARKS

Upon entry of the amendments herein, claims 2-9 are pending in the application. Claim 1 has been canceled and claims 2-9 have been amended. Also, several amendments have been made to the specification. No new matter has been introduced by any of the amendments herein.

The Examiner has acknowledged Applicants' claim for foreign priority but has noted that a certified copy of the priority application has not been submitted. Applicants provide herewith a certified copy of Indian application No. 1019/MAS/98.

The Examiner asserts that "[T]he title of the invention should be placed at the top of the first page of the specification;" Applicants wish to point out that that is where the title can already be found. However, said title has been replaced by amendment herein with the amended one entered during the International Stage of this application. The new title was actually already assigned to the application as evidenced by the Filing Receipt.

At the Examiner's request, the heading "Brief Description of the Drawings" has been inserted before the descriptions of Figures 1-8 found on page 9 of the instant specification as filed. Furthermore, in accordance with 37 CFR §1.77, the entire section has effectively been moved from its original location on page 9 to the position, beginning on page 4, between the "Brief Description of the Invention" and the "Detailed Description of the Invention" sections. At the Examiner's request, the "Detailed Description" section, already present in the

application and fully conforming to the requirements stated in the Office Action, has been identified as such by insertion of the appropriate heading at the beginning of the section. Furthermore, the "Brief Summary of the Invention" section, also already present in the application, has been identified as such by insertion of the appropriate heading at its beginning.

Claims 6-9 have been objected to under 37 CFR §1.75(c) as being improperly multiply dependent. All of these claims have been amended to depend solely from claim 2 and are now proper dependent claims.

The rejection of claim 1 as indefinite is moot in light of its cancellation.

Responsive to the Examiner's rejection of claim 2 for reciting the acronym "UDP," said acronym has been replaced by the full term (see page, 4, lines 12 and 13 of the specification) in the claim.

With respect to the indefiniteness rejection of claim 2 on the ground of alleged omission of essential steps, Applicants wish to direct the Examiner's attention to page 6, lines 16-24 of the instant specification, which passage clearly discloses the relationship between the measurement of light energy and the detection of peptidoglycan synthesis. As disclosed in the specification prior to this passage, UDP-*N*-acetyl-glucosamine is a precursor in the synthesis of peptidoglycan, and said precursor, as used in the instant assay, is radiolabeled.

In the above cited passage on page 6, it is explained that, through the binding of [the radiolabeled] peptidoglycan (formed

under the conditions of the assay (see step (1) of claim 2)) to the lectin-coated beads impregnated with the fluorescer substance, the radiolabel is brought into close proximity with the fluorescer. The presence of the radioactivity causes the fluorescer to fluoresce and so emit light energy that can be measured by suitable means. Thus, if peptidoglycan is formed, the fluorescer will be activated and light emitted, but if peptidoglycan is not formed (for example, because of the presence of an enzyme inhibitor), then the fluorescer is not activated and no light is emitted. Accordingly, the allegation of indefiniteness of claim 2 on this basis is without merit and should be withdrawn.

Further with respect to claim 2, the Examiner asserts that it is confusing as to whether it is "the 'source' or the element following the term 'source', [which] is a part of the claimed invention." Applicants emphatically disagree with this assertion; the stated ground of rejection is without merit.

Applicants note, in the first place, that the Examiner cites MPEP §2173.05(d). This section deals with the recitation in a claim of a limitation followed by recitation in the same claim of an example or a preferred embodiment further limiting the original limitation (e.g. "R is halogen, for example, chlorine"). The instantly rejected claim presents no such situation. The Examiner erroneously opines that the present claim language is in the same category as that treated in §2173.05(d) and thus, for example, in connection with the phrase "source of divalent metal ions," that "divalent metal ions" represents a further limitation

of "source." However, this is an inappropriate assessment. While the Examiner may find such language confusing, certainly no one of ordinary skill in the art would find it so, and Applicants should not be penalized accordingly.

Claim 2 does not recite, e.g., "a source, for example a source of divalent metal ions" or any such similar phraseology. In the present context and even in more general English usage, "a source of X" must be regarded as a single descriptive element; the 2 parts of the phrase cannot be segregated in the way the Examiner implies in invoking §2173.05(d). The source and what the source provides are, for the purpose of carrying out the invention, indistinguishable.

In the present context, one of ordinary skill in the art or for that matter anyone, skilled or otherwise, reading the application, would understand that, for example, divalent metal ions are required in the reaction mixture (assay step (1)) used to carry out the assay. Thus some "source," i.e., something providing these ions, is required. Any "source" that provides these ions is suitable for the practice of the invention. Similarly, it would be clear to anyone reading instant claim 2 that the reaction mixture requires, in addition to divalent metal ions, undecaprenyl phosphate, peptidoglycan, translocase enzyme, transferase enzyme, transglycosylase enzyme, transpeptidase enzyme and pyrophosphorylase enzyme. Thus, the phrase "source of...," whether it be of divalent metal ions or any of the other recited components of the assay reaction mixture, must be

regarded as a single limitation and not a limitation within a limitation.

Furthermore, the specification provides an example of what a "source of divalent metal ions" could be (the Examiner is directed to page 5, lines 11 and 12 of the specification). Still further, page 5, lines 14 to 19 of the specification, provides guidance as to a preferred source of the other assay reaction mixture components. However, again, it should be emphasized that these disclosures are merely exemplary, and the efficient practice of the invention does not depend on the identification of particular sources but on the availability of the particular ingredients, e.g., divalent metal ions, undecaprenyl phosphate, etc., provided by their respective sources, whatever those sources might be. Applicants also wish call the Examiner's attention to claim 4, which is further limiting of claim 2 and recites a source of various of the assay reaction mixture components. As with the previously discussed ground of rejection of claim 2 as indefinite, this rejection is without merit and should be withdrawn.

Claims 3, 4 and 5 have been amended as the Examiner has suggested to provide them with proper antecedent basis. Claims 6-9 have been amended in the same way.

Claims 1-5 have been rejected Under 35 USC §103(a) as obvious over published International Application WO 96/05258 of Elhammer et al. in view the articles of Mengin-Lecreaux et al. and Kohlrausch et al.

The Examiner asserts that the Elhammer disclosure of a scintillation proximity assay (SPA) and its further disclosure of specific components of the assay mixture combined with disclosure by Mengin-Lecreaux et al. and Kohlrausch et al. regarding peptidoglycan synthesis, render obvious the instantly claimed invention. Applicants disagree with this assessment.

The Elhammer reference describes the application of SPA technology to a mammalian sugar transferase reaction. The reaction is catalyzed by an enzyme, Gal*N*Ac-transferase, which, although normally membrane bound, is used in soluble form, as this is said to avoid complications (see page 3, lines 12-15).

The reference teaches the use of various different types of SPA beads. The beads may be lectin-coated as in the present invention. Thus, on lines 30-34 of page 8, an embodiment is disclosed in which the enzyme, Gal*N*Ac-transferase, catalyzes the transfer of ^{3}H-Gal*N*Ac from UDP-^{3}H-Gal*N*Ac to an acceptor peptide and the glycosylated product formed is adsorbed onto SPA beads coated with a Gal*N*Ac-specific lectin.

It must be appreciated, then, that the disclosure of Elhammer is highly specific and certainly does not provide any general teaching of the use of SPA technology and lectin-coated beads in other types of assays, let alone an assay for detecting peptidoglycan synthesis. Indeed, there is nothing in Elhammer which might suggest that lectin-coated beads could be efficaciously used to capture peptidoglycan or bacterial membranes (if these are used as a source of peptidoglycan), which is an important aspect of the assay of the present invention.

The fact that the beads can be so used is most surprising and could not have been predicted from the disclosure of Elhammer. Moreover, unlike the Elhammer system, membrane-bound enzymes may be used advantageously in the present invention as set forth in Example 1 of the present specification. One of skill in the art would have had no motivation to try or use the Elhammer system for the purpose of implementing the presently claimed assay.

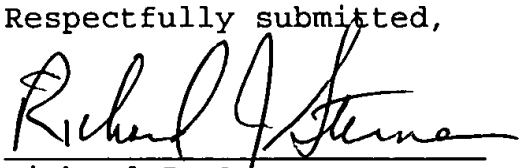
Accordingly whatever particular details are alleged by the Examiner to be provided by the Mengin-Lecreaux and Kohlrausch disclosures, said disclosures cannot make up for the fundamental gaps in the disclosure of Elhammer et al. Even if the secondary references do disclose some details of the pathway of peptidoglycan synthesis, and even if some of these details could truly be labeled "inherent," the references do not fill in for the silence of the primary reference with respect to the fundamental combining of SPA and fluorescent bead technologies for the purpose of carrying out an assay such as that recited in the instant claims. Neither the Elhammer disclosure alone nor in combination with the secondary references provides sufficient guidance or motivation to lead one of skill in the art to the present invention; this rejection should be withdrawn.

The above amendments and remarks properly address all of the Examiner's formal rejections as well as those based on allegations of indefiniteness and obviousness. Reconsideration and allowance of pending claim 2-9 are respectfully requested.

The Assistant Commissioner is hereby authorized to charge any fees which may be due for any reason to Deposit Account No. 23-1703.

Dated: August 13, 2001

Respectfully submitted,



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Enclosures

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

Paragraph running from line 17 through line 25 of page 2:
In the third stage, at the exterior of the cytoplasmic membrane, polymerisation of the glycan occurs. The disaccharide-pentapeptide unit is transferred from the lipid carrier to an existing disaccharide unit or polymer by a peptidogycan transglycosylase (also referred to as a peptidoglycan polymerase) (hereafter referred to as "the transglycosylase"). The joining of the peptide bridge is catalyzed by peptidoglycan transpeptidase (hereafter referred to as "the transpeptidase"). Both enzyme activities, which are essential, reside in the same molecule, the penicillin-binding proteins (or PBPs), as in PBP 1a or 1b in *Escherichia coli*. These are the products of the ponA and ponB genes respectively, in *Escherichia coli*.

In the claims:

2. (amended) An assay for detecting peptidoglycan synthesis, which comprises the steps of:
(1) incubating a reaction mixture comprising in aqueous medium a uridine(5'-)diphoshate (UDP)-*N*-acetylmuramylpentapeptide, radiolabelled UDP-*N*-acetyl glucosamine, a source of divalent metal ions, a source of undecaprenyl phosphate, a source of peptidoglycan, a source of translocase enzyme, a source of transferase enzyme, as source of transglycosylase enzyme, a source of transpeptidase enzyme and a source of lipid

pyrophosphorylase enzyme, under conditions suitable for peptidoglycan synthesis;

(2) adding a divalent metal ion chelator compound to the reaction mixture of step (1);

(3) adding lectin-coated beads impregnated with a fluorescer to the reaction mixture of step (2); and

(4) measuring light energy emitted by the fluorescer.

3. (amended) [An] The assay according to claim 2, wherein the UDP-*N*-acetylmuramylpentapeptide is UDP-Mur*N*Ac-L-alanine-γ-D-glutamic acid-m-diaminopimelic acid-D-alanine-D-alanine.

4. (amended) [An] The assay according to claim 2 or claim 3, wherein bacterial cell membranes represent a source of one or more of undecaprenyl phosphate, peptidoglycan, translocase enzyme, transferase enzyme, transglycosylase enzyme, transpeptidase enzyme and lipid pyrophosphorylase enzyme.

5. (amended) [An] The assay according to claim 4, wherein the bacterial cell membranes are from *Escherichia coli*.

6. (amended) [An] The assay according to [any one of claims 2 to 6] claim 2, wherein the reaction mixture of step (1) further comprises a test compound.

7. (amended) [An] The assay according to claim 6, wherein the test compound is an antagonist of one of the enzymes.

8. (amended) [An] The assay according to [any one of claims 2 to 7] claim 2, wherein ethylenediaminetetraacetic acid is used as the divalent metal ion chelator compound in step (2).

9. (amended) [An] The assay according to [any one of claims 2 to 8] claim 2, wherein the lectin-coated beads comprise [wheatgerm] wheat germ agglutinin.